REMARKS

Claim 76 is pending in the instant application and is currently subject to (1) a rejection under 35 U.S.C § 102(b) in light of US Patent 5,538,733 to Emery et al. ("Emery") and (2) a rejection under 35 U.S.C. § 102(b) in light of US Patent 5,593,697 to Barr et al. ("Barr"). Applicants respectfully request that the following remarks be made part of the record in the file history of the instant application.

I. Rejection Under 35 U.S.C. § 102(b) Should be Withdrawn

Claim 76 is rejected under 35 U.S.C. § 102(b) as being anticipated by Emery as well as Barr.

In particular, the Examiner asserts that Emery discloses an implant that incorporates antigens in a time-delay matrix. The Examiner alleges that the implants have a matrix structure that allows for the incorporation of an antigen and for its release at a desired rate and thus Emery provides for an implant with a means of limiting the passive diffusion of antigens from the porous matrix without limiting the movement of immune cells into the device.

Further, the Examiner states that Barr discloses a pharmaceutical implant that releases a pulse of biological material at a time interval after implantation. The Examiner alleges that the polymer film coating and excipient core of the Barr device are the same as the means of limiting passive diffusion and porous matrix of the current invention.

The Applicants respectfully disagree for the reasons discussed below.

A. The Legal Standard

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). "Anticipation under Section 102 can be found only if a reference shows exactly what is claimed . . ." *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707 (Fed. Cir. 1984).

B. **The Invention**

The present invention relates to a method of immunizing a mammal for the preparation of hybridomas for the production of monoclonal antibodies against an antigen. The method involves implanting within a mammal a device that has a porous matrix that contains an antigen within a container having a means for limiting passive diffusion of an antigen or immune cell secretory or co-stimulatory factors out of the device. This diffusion barrier maintains optimal levels of antigen, immune cell secretory products and immune cells within the device. Page 14, lines 2-7.

C. **The Claimed Invention Is Not Anticipated By Emery**

Examiner asserts that the Claim 76 of the current application is anticipated by Emery. However, as noted in Applicants' reply of December 20, 2007, Emery does not disclose each of the limitations of the current claims. Namely, Emery does not disclose a container for the porous matrix, and thus Emery fails to anticipate the presently claimed device since it lacks the container with the means for limiting the passive diffusion of antigens and immune cell secretory products and co-stimulatory factor out of the device.

First, within the presently claimed device the matrix and the container serve different purposes. The porous matrix, *i.e.*, a sponge-like material, of the device acts as a depository for the antigen. The antigen can either be incorporated into the matrix or injected into the matrix prior to or after implantation. (Page 19, line 21 to Page 20, Line 12). The container, however, is a coating surrounding the matrix that acts has means for limiting the diffusion of the antigen out of the device. (Page 20, Line 13 to Page 23, Line 7). The container is less porous than the matrix to achieve a balance between permitting the active recruitment of immune cells into the device while preventing the passive diffusion of antigens and small molecules such as co-stimulatory factors (cytokines produced by immune cells within the device) out of the device. The device of the present invention generates a robust immune response since subsequent immune cells are primed when they come into contact with the antibody of interest or the various small molecules concentrated within the device. The diffusion barrier of the device optimizes

the development of an immune response to the antigen by maintaining a high concentration of antigens and small molecules within the device and this also imparts long-term immunity by producing a population of memory cells. Thus, the matrix and the container of the present device are not one in the same.

Emery does not anticipate an implant having a container with means of limiting diffusion of the present invention. As Applicants previously noted, Emery does not disclose an implant having a container with means of limiting diffusion. Emery discloses a solid implant comprised of biocompatible, biodegradable, bioabsorbable and/or bioerodible polymeric material that will release an immunogenic agent for sustained delivery into the surrounding tissue fluids. (Col. 2, Line 15-37). Emery teaches the release of antigens into the surrounding tissues as opposed to retaining a concentration of antigens within the device, and therefore the use of a container that has means of limiting diffusion would be contrary to the aims of the Emery implant. However, in the implant of the present invention, "the antigen is retained within the device and its concentration remains high, as do the concentrations of co-stimulatory factors secreted by the cell population with[in] the device, much in the same fashion as within a lymph node." (Page 14, Lines 20-22) The present invention utilizes the container with means of limiting diffusion to limit the passive diffusion of the antigens out of the device and thereby maintain a high concentration of antigens and small molecules within the device. Thus, Emery does not disclose the use of a container having means of limiting diffusion and fails to anticipate the presently claimed invention.

Accordingly, applicants respectfully submit that the 35 U.S.C. § 102 rejection for Emery has been overcome and request their withdrawal.

D. The Claimed Invention Is Not Anticipated By Barr

As noted above, the Examiner asserts that Barr anticipates Claim 76. However, contrary to the Examiner's assertion the Barr implant does not have a container that has means of limiting the diffusion of antigens, cell secretory products or co-stimulatory factors given that the container in Barr is continuous and therefore lacks any means for diffusion.

The Barr device is concerned with a biocompatible or biodegradable implant for the

administration of antigens in a pulse released fashion, in which the antigen contacts tissue in the host animal, at a period of time after implantation. (Col. 1, lines 7-11). The Barr device is comprised of (a) a biologically active material, (b) an excipient comprising at least one water soluble material and at least one water insoluble material, and (c) a polymer film coating adapted to rupture at a predetermined time after implantation. (Col. 3, lines 30-42). According to Barr, the polymer film is a biocompatible bilayer film capable of forming an impermeable barrier to the antigen (isolating the antigen from physiological fluid) until the inner layer of the film fails. (Col. 5, lines 2-5). Specifically, the polymer film consists of an insoluble outer layer, whose thickness controls the timing and degree of access of physiological fluid to the inner layer, and an inner layer, which is soluble at physiological pH. (Col. 5, lines 5-11). The failure of the inner layer of the film permits the physiological fluid to access the excipient, which according to Barr consists of water soluble and insoluble excipients. The water insoluble excipient acts as a swellable excipient which exerts pressure sufficient enough to rupture the impermeable outer film. (Col. 5, lines 11-14.)

Barr does not contain a diffusion barrier as taught by the current invention. As noted in the specification of the above-noted application, the container maintains a diffusion barrier in the container restricting the diffusion of antigens from the device but permit the free ingress and egress of immune and other cells out of the device through means such as perforations. (pg. 14, lines 2-7). Whereas the outer film in the Barr device forms an impermeable barrier to the antigen until such time as the inner, pH sensitive film fails due to ingress of physiological fluid (i.e., molecular weight below 1000 Daltons; Col. 6, lines 39-40). According to Barr, the thickness of this outer barrier may be varied to adjust the time to failure of the inner film. Thus, the bilayer film in the Barr device does not operate to the same effect as the container in the current device. The bilayer film in the Barr device acts as a timing device by permitting the release of antigen at a point in the future when the film fails, whereas the perforated container in the current invention acts as a selective barrier permitting during its operation the ingress and egress of immune cells within the device while restricting the release of antigen from the device during the useful life of the device

In view of the remarks above, the Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) in light of Barr.

CONCLUSIONS

Applicants respectfully request that the foregoing remarks be made of record in the file history of the instant application. Applicants submit that the remarks and amendments made herein now place the pending claims in condition for allowance. If a telephone discussion will help expedite processing of this application, the Examiner is invited to telephone the undersigned at (914) 762-7586.

Respectfully submitted,

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